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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/900,355	07/06/2001	H. Craig Dees	PHO-122	5998

7590

02/07/2003

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 02/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/900,355

Applicant(s)

DEES ET AL.

Examiner

Janet L Epps-Ford, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 December 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) 12-18 and 28-30 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-11, 19-27 and 31-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3, 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election of group I in Paper No. 10 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).
2. Claims 12-18, and 28-30 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 10.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 3-8, 19, 21-26, and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Goers et al.

Goers et al. disclose the use of photochemicals including photosensitizers, wherein said photosensitizers include xanthenes and in particular Rose Bengal, as therapeutic agents (col. 20, lines 50-55). Additionally, in another embodiment, Goers et al. teach that antibodies may be covalently attached to the therapeutic agents (i.e. photosensitizers including Rose Bengal) of Goers et al. through an intermediate linker (see col. 21, lines 9-13). Moreover, Goers et al. teach that the antibody or antibody fragment of the antibody therapeutic agent conjugate functions to deliver the conjugate to the target site, i.e. the antibody functions as a targeting moiety (see col.

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28, lines 5-17). Moreover, Goers et al. describe the use of the antibody-therapeutic agent conjugate in photoradiation therapy, which encompasses the treatment of disorders by combining the phototoxic effects of the photosensitizer and the site-specific attachment of the antibody to a target site (col. 28, lines 45-68).

The choice of antibodies, linkers, and compounds used to make the conjugates depends upon the purpose of delivery. The delivery and release or activation of therapeutic agents at specific target sites may result in selective killing or inhibition of proliferation of tumor cells, (col. 28, lines 18-23), therefore they can be used for chemotherapeutic purposes.

In the preparation of antibody therapeutic agent conjugates a *solution* of the oxidized antibody at a concentration of from about 0.5 to 20 mg/ml is mixed with the therapeutic agent or linker (molar ratios of reactive amine group to antibody aldehyde ranging from about 1 to about 10,000) and the solution incubated for from about 1 to 18 hours. Therefore the antibody-conjugate is in is liquid or aqueous solution (see col. 17, lines 29-34).

Goers et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

5. Claims 1-11, 19-27, and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Bottiroli et al. (WO97/03697 A2).

Bottiroli et al. teach fluorogenic substrates suitable for diagnosis and photodynamic treatment of tumours. These substrates comprise, for example, the Rose Bengal derivative Rose Bengal acetate (page 4, lines 1-5). (According to the specification as filed, page 2, paragraph [0005], "the halogenated xanthene is Rose Bengal or a functional derivative of Rose Bengal.") The acetate group forms an ester with the Oxygen atom attached to the #6 Carbon of Rose

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Bengal, this ester linkage is cleaved by in the presence of the esterase enzyme particularly present in tumor cells (page 5, lines 22-26).

Bottiroli et al. teach that the fluorogenic substrates can be administered for the treatment of tumors comprising a dose varying from 1-to 10 mg/kg b.w. (i.e. halogenated xanthene is present in a concentration greater than about 0.0001% to less than about 20%), and administration can be systemic in the form of an isotonic saline solution, or as a suspension liposomes. The intracavitary route can administer the same preparation. Topical application requires the use of a water solution with the addition of substances favoring the absorption and penetration of the active principle (page 11, lines 1-14).

Bottiroli et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

6. Claims 1, 3-6, 19, 21-24, and 31-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Schultz et al.

Schultz et al. disclose novel polypeptides having at least one active functionality, wherein the active functionality may be a reporter molecule (col. 4, lines 58-70), wherein the active functionality may be linked to the polypeptide via a cross linking agent (col. 8, lines 50-70). A wide variety of fluorescers may be employed either by themselves or in conjunction with quencher molecules as active functionalities. In one particular embodiment, the fluorescers include xanthene (col. 9, line 66), and more specifically may include Rose Bengal (col. 10, line 26).

Schultz et al. teach each and every aspect of the instant invention thereby anticipating Applicant's claimed invention.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2 and 20 are rejected under 35 U.S.C. 103(a) as being obvious over Goers et al.

The discussion of Goers et al. set forth above is incorporated here. Goers et al. does not disclose the same percent concentration of halogenated xanthene used in the medicaments of the present invention. However, the recitation of a specific percent, ratio or range does not render any patentable weight if the prior art discloses the claimed compositions, absent evidence of unexpected results with regards to the claimed range, percent or ration. See MPEP § 2144.05 which states that "[G]enerally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by

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routine experimentation.”

Therefore, the invention as a whole would have been prima facie obvious at the time of filing over Goers et al.

Double Patenting

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 1-11, 19-27 and 31-33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-10, 12-19, 21-30, 32-34, and 36-38 of copending Application No. 09/635,276, and claims 1-44 of copending Application No. 09/799,785. Although the conflicting claims are not identical, they are not patentably distinct from each other because both the claims of the instant application and those of the co-pending applications are drawn to compositions comprising a halogenated xanthene compound, and methods of treating human or animal tissue. Although the compositions of the instant claims and those recited in the claims of the co-pending applications recite different "intended uses," the compositions themselves comprise the same elements, i.e. a composition comprising a halogenated xanthene compound or further comprising a targeting moiety, and would therefore necessarily possess identical properties and uses. In the instant

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case, the recitation of intended use of the claimed compositions does not function as a limitation that must be considered for patentability purposes since it does not appear that the recited "intended use" results in a structural difference between the claimed invention recited in the instant claims and that recited in the co-pending applications. See MPEP § 2111.02.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

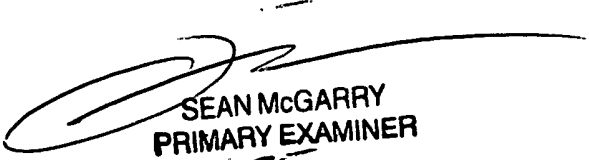
12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L Epps-Ford, Ph.D. whose telephone number is 703-308-8883. The examiner can normally be reached on M-T, Thurs-Friday 9:00AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-746-5143 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Janet L Epps-Ford, Ph.D.
Examiner
Art Unit 1635

JLE
February 3, 2003


SEAN MCGARRY
PRIMARY EXAMINER
1635